

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-39: Cancelled.

40. (Withdrawn and previously amended): An attenuated human rotavirus population, comprising a single variant or substantially a single variant, said variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7, wherein said VP4 single variant or substantially single variant is chosen from the group of: a VP4 variant, wherein the VP4 gene contains a thymine base (T) at position 501 from the start codon; and a VP4 variant, wherein the VP4 gene encodes a VP4 protein that contains a phenylalanine (Phe) at position 167 from the start codon; and wherein said VP7 single variant or substantially single variant is chosen from the group of: a VP7 variant, wherein the VP7 gene contains a thymine (T) at position 605 from the start codon; and a VP7 variant in which the VP7 gene codes for a VP7 protein that contains a methionine (Met) at position 202 from the start codon .

41. (Withdrawn): A rotavirus population according to claim 40 which is a cloned strain.

42. (Withdrawn): A rotavirus population according to claim 40 which is derived from a human rotavirus infection.

43. (Withdrawn): A rotavirus population according to claim 40 which replicates in and is excreted by humans.

44. (Withdrawn): A rotavirus population according to claim 40 in which the substantially single variant is a variant in which the VP4 gene comprises at least one substitution chosen from the group of: an adenine base (A) at position 788; an adenine base (A) at position 802; and a thymine base (T) at position 501 from the start codon.

45. (Withdrawn): A rotavirus population according to claim 44 in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1.

46. (Withdrawn): A rotavirus population according to claim 40 in which the substantially single variant is a variant in which the VP7 gene comprises at least one substitution chosen from the group of: a thymine (T) at position 605; an adenine (A) at position 897; and a guanine (G) at position 897 from the start codon.

47. (Withdrawn): A rotavirus population according to claim 46 in which the VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.

48. (Withdrawn): A rotavirus population according to claim 40 in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1, and the VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.

49. (Withdrawn): A rotavirus which comprises a nucleotide sequence encoding a VP4 protein wherein the nucleotide sequence is the nucleotide sequence set forth in SEQ ID NO:1, and a nucleotide sequence encoding a VP7 protein.

50. (Withdrawn): A rotavirus population according to claim 40, designated as P43 and deposited under accession number ECACC 99081301.

51. (Withdrawn): A rotavirus variant designated P43 and deposited with the ECACC under accession number 99081301, rotavirus progeny and immunologically active derivatives thereof and materials obtained therefrom.

52. (Withdrawn): A rotavirus reassortant comprising at least one antigen or at least one segment of the rotavirus variant P43 of claim 50.

53. (Withdrawn): A method of producing a purified human rotavirus population comprising a substantially single variant, the method comprising:
passaging a rotavirus preparation on a suitable cell line;
optionally selecting homogeneous culture using the steps of either:
limit dilution; or
individual plaque isolation; and
checking for the presence of a substantially single variant by sequencing an appropriate region of the VP4 and/or VP7 gene sequence.

54. (Withdrawn): A method according to claim 53 in which the rotavirus preparation is passaged on AGMK cells.

55. (Withdrawn): A method according to claim 53 in which the rotavirus preparation has the characteristics of an 89-12 strain or derivative thereof.

56. (Withdrawn): A method according to claim 53, which comprises the additional step of ether treatment to remove adventitious ether-sensitive contaminating agents.

57-76: (Cancelled)

77. (Withdrawn): A method of manufacture of a rotavirus vaccine comprising admixing a lyophilized live attenuated human rotavirus with an antacid and a viscous agent.

78. (Withdrawn): A method of preventing rotavirus infection in humans by administering to a human subject in need thereof an effective amount of a vaccine according to claim 57.

79-81: (Cancelled)

82. (Currently amended): A vaccine composition comprising a live attenuated human rotavirus population ~~according to claim 57~~ comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant, in which the single variant or substantially single variant is a variant in which the VP4 gene comprises at least one substitution chosen from the group of: an adenine base (A) at position 788; an adenine base (A) at position 802; and a thymine base (T) at position 501 from the start codon.

83. (Currently amended): ~~A~~ The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein ~~in which~~ the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1.

84. (Currently amended): A vaccine composition comprising a live attenuated human rotavirus population ~~according to claim 57~~ comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant, in which the single variant or substantially single variant is a variant in which the VP7 gene comprises at least one substitution chosen from the group of: a thymine (T) at position 605, an adenine (A) at position 897, and an adenine (A) at position 108 ~~a guanine (G) at position 897~~ from the start codon.

85. (Currently amended): ~~A~~ The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein ~~in which~~ the VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.

86. (Currently amended): A vaccine composition comprising a live attenuated human rotavirus population ~~according to claim 57~~ , comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant, in which the VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1, and the VP7 gene comprises a nucleotide sequence set forth in SEQ ID NO:2.

87. (Currently amended): A vaccine composition comprising a live attenuated rotavirus ~~which~~ that comprises a nucleotide sequence encoding a VP4 protein, wherein said VP4-encoding nucleotide sequence comprises the nucleotide sequence set forth in SEQ ID NO:1, and a nucleotide sequence encoding a VP7 protein.

88. (Currently amended): A vaccine composition comprising a live attenuated rotavirus ~~which that~~ comprises a nucleotide sequence encoding a VP4 protein and a nucleotide sequence encoding a VP7 protein, wherein said VP7-encoding nucleotide sequence is set forth in SEQ ID NO:2.

89. (Currently amended): A vaccine composition comprising a live attenuated human rotavirus population ~~according to claim 57, comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant~~, designated as P43 and deposited under accession number ECACC 99081301.

90. (Previously presented): A vaccine composition comprising a live attenuated rotavirus variant designated P43 and deposited with the ECACC under accession number 99081301, rotavirus progeny and immunologically active derivatives thereof and materials obtained therefrom.

91. (Previously presented): A vaccine composition comprising a live attenuated rotavirus reassortant comprising at least one antigen or at least one segment of the rotavirus variant P43 of claim 89.

92. (Currently amended): A vaccine composition comprising a live attenuated human rotavirus population ~~according to claim 57, comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant~~, in which the single variant or substantially single variant is a variant in which the VP4 gene encodes a VP4 protein, wherein a phenylalanine (Phe) is present at position 167 from the start codon.

93. (Currently amended): A vaccine composition comprising a live attenuated human rotavirus population ~~according to claim 57, comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding at least one of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant~~, in which the single variant or substantially single variant is a variant, wherein the VP7 gene encodes a VP7 protein in which a methionine (Met) is present at position 202 from the start codon.

Please add the following new claims:

94. (New) A vaccine composition comprising a live attenuated human rotavirus population, comprising a single variant or substantially a single variant defined by a nucleotide sequence encoding both of the major viral proteins designated as VP4 and VP7 in a suitable pharmaceutical carrier or adjuvant, in which the substantially single variant is a variant in which the VP4 gene comprises the following three substitutions: an adenine (A) at

position 788; an adenine (A) at position 802; and a thymine (T) at position 501 from the start codon, and wherein the single variant or substantially single variant is a variant in which the VP7 gene comprises the following three substitutions: a thymine (T) at position 605, an adenine (A) at position 897, and an adenine (A) at position 108 from the start codon.

95. (New): The vaccine composition according to claim 82, wherein said composition is adapted for oral administration.

96. (New): The vaccine composition according to claim 95, wherein said live attenuated virus is formulated with an antacid composition.

97. (New): The vaccine composition according to claim 96, wherein said antacid composition comprises an organic antacid.

98. (New): The vaccine composition according to claim 97, wherein said organic antacid is sodium citrate.

99. (New): The vaccine composition according to claim 96, wherein said antacid composition comprises an inorganic antacid.

100. (New): The vaccine composition according to claim 99, wherein said inorganic antacid is aluminium hydroxide.

101. (New): The vaccine composition according to claim 99, wherein said inorganic antacid is calcium carbonate.

102. (New): The vaccine composition according to claim 101, wherein said composition further comprises a viscous agent.

103. (New): The vaccine composition according to claim 102, wherein said viscous agent is xanthane gum.

104. (New): The vaccine composition according to claim 103, wherein said live attenuated virus is formulated with calcium carbonate and xanthane gum and reconstituted with aqueous solution.

105. (New): The vaccine composition according to claim 96, wherein said live attenuated virus is formulated with the antacid composition and lyophilized in a blister pack.

106. (New): The vaccine composition according to claim 82, wherein said virus is in lyophilized form.

107. (New): The vaccine composition according to claim 106, wherein said live attenuated virus and said antacid composition are present in separate containers for formulation as a liquid vaccine composition prior to administration.

108. (New): The vaccine composition according to claim 106, wherein said live attenuated virus and said antacid composition are present in the same container formulated as a lyophilized vaccine composition.

109. (New): The vaccine composition according to claim 106, wherein said composition is for administration on the tongue of a patient, and wherein said composition is in the form of a quick-dissolving tablet for immediate dissolution when placed on the tongue of the patient.

110. (New): The vaccine composition according to claim 106, further comprising a lyophilized live attenuated rotavirus and an inorganic antacid, such as calcium carbonate, and a viscous agent, such as xanthane gum.

111. (New): The vaccine composition according to claim 110, wherein said attenuated virus and said antacid composition are present in separate containers for formulation as a liquid vaccine composition prior to administration.

112. (New): The vaccine composition according to claim 110, wherein said attenuated virus and said antacid composition are formulated in the same container, as a lyophilized vaccine composition.

113. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein said rotavirus population is a cloned strain.

114. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein said rotavirus population is derived from a human rotavirus infection.

115. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein said rotavirus population replicates in, and is excreted by, humans.

116. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein said variant or substantially single variant further comprises a variant of the VP7 gene that comprises at least one substitution chosen from the group of: a thymine (T) at position 605, an adenine (A) at position 897, and an adenine (A) at position 108 from the start codon.

117. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein said variant or substantially single variant is a

variant in which said VP7 gene comprises at least one substitution chosen from the group of: a thymine (T) at position 605, an adenine (A) at position 897 and a guanine (G) at position 897 from the start codon.

118. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 117, wherein said VP7 gene comprises the nucleotide sequence set forth in SEQ ID NO:2.

119. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82, wherein said VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1, and said VP7 gene comprises a nucleotide sequence set forth in SEQ ID NO:2.

120. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 82 that is designated as P43 and deposited under accession number ECACC 99081301.

121. (New): The vaccine composition according to claim 84, wherein said composition is adapted for oral administration.

122. (New): The vaccine composition according to claim 121, wherein said live attenuated virus is formulated with an antacid composition.

123. (New): The vaccine composition according to claim 122, wherein said antacid composition comprises an organic antacid.

124. (New): The vaccine composition according to claim 123, wherein said organic antacid is sodium citrate.

125. (New): The vaccine composition according to claim 132, wherein said antacid composition comprises an inorganic antacid.

126. (New): The vaccine composition according to claim 125, wherein said inorganic antacid is aluminium hydroxide.

127. (New): The vaccine composition according to claim 125, wherein said inorganic antacid is calcium carbonate.

128. (New): The vaccine composition according to claim 127, wherein said composition further comprises a viscous agent.

129. (New): The vaccine composition according to claim 128, wherein said viscous agent is xanthane gum.

130. (New): The vaccine composition according to claim 129, wherein said live attenuated virus is formulated with calcium carbonate and xanthane gum and reconstituted with aqueous solution.

131. (New): The vaccine composition according to claim 125, wherein said live attenuated virus is formulated with the antacid composition and lyophilized in a blister pack.

132. (New): The vaccine composition according to claim 84, wherein said virus is in lyophilized form.

133. (New): The vaccine composition according to claim 132, wherein said live attenuated virus and said antacid composition are present in separate containers for formulation as a liquid vaccine composition prior to administration.

134. (New): The vaccine composition according to claim 132, wherein said live attenuated virus and said antacid composition are present in the same container formulated as a lyophilized vaccine composition.

135. (New): The vaccine composition according to claim 132, wherein said composition is wherein said composition is for administration on the tongue of a patient, and wherein said composition is in the form of a quick-dissolving tablet for immediate dissolution when placed on the tongue of the patient.

136. (New): The vaccine composition according to claim 132, further comprising a lyophilized live attenuated rotavirus and an inorganic antacid, such as calcium carbonate, and a viscous agent, such as xanthane gum.

137. (New): The vaccine composition according to claim 136, wherein said attenuated virus and said antacid composition are present in separate containers for formulation as a liquid vaccine composition prior to administration.

138. (New): The vaccine composition according to claim 136, wherein said attenuated virus and said antacid composition are formulated in the same container, as a lyophilized vaccine composition.

139. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein said rotavirus population is a cloned strain.

140. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein said rotavirus population is derived from a human rotavirus infection.

141. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein said rotavirus population replicates in, and is excreted by, humans.

142. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein the single variant or substantially single variant further comprises a variant of the VP4 gene that comprises at least one substitution chosen from the group of: an adenine (A) at position 788; an adenine (A) at position 802; and a thymine (T) at position 501 from the start codon.

143. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein said VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1.

144. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84, wherein said VP4 gene comprises the nucleotide sequence set forth in SEQ ID NO:1, and said VP7 gene comprises a nucleotide sequence set forth in SEQ ID NO:2.

145. (New): The vaccine composition comprising a live attenuated rotavirus population according to claim 84 that is designated as P43 and deposited under accession number ECACC 99081301.